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Nasopharyngeal flora in HIV seropositive men who have sex with men

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Objectives: To assess, in men who were infected with the human immunodeficiency virus (HIV) and who identified themselves as having had sex with men; the nasopharyngeal prevalence of *Neisseria gonorrhoeae*, *N meningitidis*, *Corynebacterium diphtheriae*, and candida species; oral sexual behaviour; the relation between oral flora and oral sexual behaviour.

Method: Nasopharyngeal swabs were taken from HIV seropositive men for culture. The men were also asked to complete a self administered questionnaire.

Results: 390 men were recruited; 286 (73.3%) provided nasopharyngeal samples and questionnaires; 41 (10.5%) provided nasopharyngeal samples only; 63 (16.2%) provided questionnaires only. From the 327 nasopharyngeal samples *N meningitidis* was cultured in 49 (15%) and candida species in 165 (50.5%). Cultures for *N gonorrhoeae* and *C diphtheriae* were all negative. Data from the 349 completed questionnaires indicated that 285 men were practising oro-penile sex, over 90% did not consistently use condoms; 150 men were practising oro-anal sex, one used dental dams. In those providing both nasopharyngeal samples and sexual behaviour data meningococcal carriage was identified in 40 (17.5%) of the 228 men practising receptive oro-penile sex, compared with one (2.3%) of the 43 non-practisers ($p < 0.025$); in 21 (20%) of the 105 men practising insertive oro-anal sex, compared with 17 (12.5%) of the 136 non-practisers ($p = 0.12$). No correlation was identified between yeast carriage and oro-genital sex.

Conclusion: Oro-genital sex, usually without barrier protection, is common among HIV infected men who have sex with men. It appears to be associated with increased meningococcal carriage but is autonomous to candida species isolation. Routine screening for nasopharyngeal *N gonorrhoeae* is not deemed necessary.

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Keywords: *Neisseria meningitidis*; HIV; sexual behaviour

Introduction

Since the onset of the human immunodeficiency virus (HIV) epidemic there has been a marked change in sexual behaviour among men who have sex with men. Oro-penile sex was always common but now, in addition to the increased use of condoms for anal sex and the utilisation of other sexual practices such as oro-anal sex, it has become part of the general armamentarium in a safer sex strategy.

Neisseria meningitidis is one of the most frequent causes of bacterial meningitis, often of an epidemic type. Fortunately, its presentation as meningococcal meningitis is uncommon compared with the prevalence of the organism's asymptomatic nasopharyngeal carriage, reported as 4.9-10.6% overall, in rural and urban habitues during non-epidemic screening in Europe and the United States.^{1,2} Carriage appears to be related to close contact and may last for many weeks or months.^{2,3} Much less commonly *N meningitidis* has been isolated from the urethra,⁴⁻¹¹ cervix,^{4,7-9} and anal canal.⁷⁻¹² The prevalence of nasopharyngeal carriage varies individually but is generally higher in men compared with women^{1,2} and particularly high rates of 17.8-46.2% have been reported in male homosexual populations.¹⁰⁻¹⁴ Indeed Faur and colleagues, observing monthly prevalence rates, have identified peaks of over 60%, almost double that of the total group studied, in male homosexuals.⁹ Yeasts have been identified in approximately 22% of pharyngeal swabs from genitourinary

medicine (GUM) clinic attenders with increased rates in homosexual men (29%) and with antibiotic use (28%).¹³ Furthermore, although uncommon, non-toxicogenic *Corynebacterium diphtheriae* is almost seven times more prevalent in homosexual than in heterosexual men¹⁵ and given the recent epidemic of toxigenic strains in eastern Europe,¹⁶ may become of increasing importance particularly in the immunosuppressed host.

This is the first study to specifically examine and relate oral sexual behaviour and nasopharyngeal flora in HIV infected men who have sex with men. This will prove critical in determining how to balance the relative low risk of HIV transmission via oro-genital sex with the transmission risks of other nasopharyngeal bacteria.

Aims

To identify the prevalence of *N gonorrhoeae*, *N meningitidis*, *C diphtheriae*, and candida species in the nasopharynx of HIV infected men who have sex with men; to assess oral sexual behaviour; to correlate any pattern between flora and behavioural practice.

Method

Nursing or medical staff recruited HIV seropositive men who were attending a large HIV outpatient unit for either planned review or unbooked assessment. All male attenders at

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Table 1 Sexual practice and absolute CD4 cell count

	Oro-penile sex		Oro-anal sex		Peno-anal sex	
	Yes (n = 285)	No (n = 58)	Yes (n = 150)	No (n = 188)	Yes (n = 221)	No (n = 125)
Mean CD4 count ($\times 10^6/l$)	293.27	172.29	312.58	243.90	311.96	200.72
t test (two tailed)	p < 0.001		p < 0.01		p < 0.001	

n = Number of question responders.

the unit were asked if they were willing to participate in a study aimed at recruiting HIV seropositive men who had sex with men to obtain data on sexual behaviour and assess nasopharyngeal flora. None had attended requesting screening for sexually transmitted diseases (STDs). Men who identified as heterosexual self deselected. Thirty eight men who were eligible declined to join the study. Informed consent was obtained from all participants. The study period spanned 3 months.

Two nasopharyngeal Amies swabs (Bibby Sterilin Ltd) were taken from each man and plated within 3 hours onto culture media. The first swab was plated onto New York City medium (VCAT) (bioMerieux) to determine the prevalence of *Neisseria* species. After 48 hours' incubation at 37°C, in 7% carbon dioxide, colonies were examined with oxidase strips. Oxidase positive Gram negative cocci were further identified using APINH QuadFerm (bioMerieux). The second swab was plated onto sheep blood agar, Hoyle's medium (Oxoid), and Sabouraud's medium (MAST Diagnostics) to identify normal oral flora, *C diphtheriae*, and candida species, respectively. After 48 hours' aerobic incubation, at 37°C, normal flora were identified as present or absent. Black colonies on Hoyle's medium were further identified by subculturing on Tinsdale's medium (Oxoid). Yeast colonies isolated on Sabouraud's medium were identified by Gram stain and wet preparation.

All men were asked to complete a self administered questionnaire. The majority completed it while alone in the clinic waiting room but one third completed it while in a private room or at home. The questionnaire aimed to obtain demographic data; details of sexual partners (regular, casual, HIV status); details of sexual behaviour and condom use over the previous 3 months; and to rank the risk of HIV transmission with different sexual

activities. A written definition of "regular" and "casual" partners was incorporated into the questionnaire and explained verbally where necessary. This was as follows: "A regular partner is one with whom sex has taken place on more than one occasion, and is characterised by some degree of sexual commitment." "A casual partner is one in which there has been no sexual commitment made, and there is no expectation of sex happening again (for example 'one night stands')." In questions appertaining to condom use the choice of "always", "sometimes", or "never" was used.

Culture and behavioural data were analysed to identify any correlations.

Results

Three hundred and ninety men, CDC stage I-IV, were recruited, 286 provided both nasopharyngeal samples and completed questionnaires (group A), 41 provided nasopharyngeal samples only (group B), and 63 completed only the questionnaire (group C). Only two had pharyngeal symptoms.

All 327 nasopharyngeal samples (groups A and B) yielded normal oral flora on culture, indicating the adequacy of sample collection. *N meningitidis* was cultured from 49 (15%) samples. Yeasts were isolated in 165 (50.5%) samples, with a light growth in 84, moderate growth in 44, and heavy growth in 37. Cultures for *N gonorrhoeae* and *C diphtheriae* were all negative.

Three hundred and forty nine questionnaires were completed (groups A and C). The data indicated that 285 men were practising oro-penile sex, of which 92.7% and 94.5%, respectively, failed to consistently, or always, use condoms when receptive with regular or casual partners; 150 men were practising oro-anal sex, only one used dental dams. There was a trend towards increased condom use for oro-penile sex with regular partners of known HIV negative status. In six of 45 (13.3%) known discordant regular relationships the HIV positive partner always used condoms for insertive oro-penile sex compared with two of 56 (3.6%) in concordant positive relationships. This did not achieve statistical significance ($p = 0.15$). Those rating oro-penile sex higher as a risk for HIV transmission, compared with those rating it lower, were significantly less likely to practise it ($p < 0.005$). There was a similar relation between the risk perceptions of oro-anal sex and its practice ($p < 0.001$). No significant relation was identified between oro-genital HIV transmission risk perceptions and the use of barrier protection ($p > 0.25$); however, it must be remembered that the overall number using protection was

Table 2 Group A – Meningococcal carriage and receptive oro-penile (O-P) and insertive oro-anal (O-A) sexual practice with casual and regular partners*

	Meningococcal carriage/ practisers of sexual behaviour	Meningococcal carriage/ non-practisers of sexual behaviour	χ^2 test (two tailed)
Receptive O-P (casual partner)	34/168 (20.2%)	5/78 (6.4%)	p < 0.025
Receptive O-P (regular partner)	28/178 (15.7%)	4/57 (7.0%)	p = 0.095
Receptive O-P (casual or regular partner)	40/228 (17.5%)	1/43 (2.3%)	p < 0.025
Insertive O-A (casual partner)	14/61 (23.0%)	25/187 (13.4%)	p = 0.074
Insertive O-A (regular partner)	11/80 (13.8%)	19/152 (12.5%)	p = 0.787
Insertive O-A (casual or regular partner)	21/105 (20.0%)	17/136 (12.5%)	p = 0.12

*Valid percentages accounting for question non-responders.

low. There was a significantly greater level of sexual activity in men with proportionately higher CD4 cell counts (table 1).

N meningitidis was isolated from 49 (15%) of the total 327 nasopharyngeal samples provided. The overall meningococcal carriage rates in groups A and B were 15.4% (44/286) and 12.2% (5/41), respectively. Associations between sexual practice and meningococcal carriage, for those with both swabs and questionnaires (group A), are shown in table 2. In view of the very small number of men always using condoms for oro-penile sex no statistical analysis of condom use and meningococcal carriage was possible. No significant relation was identified between the presence of yeasts, or their quantity, and oro-penile or oro-anal sexual practice. For example, yeasts were identified in 50.4% of individuals practising oro-anal sex compared with 48.1% of non-practisers ($p = 0.70$) and in 48.1% of individuals practising oro-penile sex compared with 55.8% of non-practisers ($p = 0.35$).

When using a self administered questionnaire of this type there is always a non-response rate where individuals fail to provide any response to a question. Hence, all of the data refer to absolute numbers and/or valid percentages based on the responders to the question or cross tabulation. Failure to appreciate this may result in perceiving data disparities.

Discussion

Among HIV infected men who have sex with men a significant association between increased meningococcal nasopharyngeal carriage and receptive oro-penile sexual practice was identified when compared with non-practising individuals. Carriage rates were also higher in those practising insertive oro-anal intercourse compared with non-practisers, but this did not achieve conventional statistical significance. Few studies have specifically examined the relation between oro-genital sex and *N meningitidis*. However, in one recent study an association was determined between meningococcal isolation and oro-genital, particularly oro-anal, sex within the preceding 2 weeks.¹³ As our data pertained to the preceding 3 months activity it is possible that the time factor may be significant and result in a modified microbiological milieu.

The presence of concurrent HIV infection, in those reporting oro-genital contact, was not associated with a higher meningococcal carriage rate than that reported in other male homosexual populations.⁹⁻¹⁴ Indeed, overall a lower meningococcal carriage rate was identified, possibly due to changes in sexual behaviour, as reduced sexual activity was reported by individuals with lower CD4 cell counts.

The clinical significance of higher meningococcal nasopharyngeal carriage rates in some HIV infected individuals has not been studied. However, for many years, epidemiologists have sought to identify the relation between asymptomatic nasopharyngeal carriage and the development of clinical meningococcal disease

within given populations. It was initially thought that outbreaks of clinical disease occurred when the carrier rate reached a critical level.¹⁷ It is now accepted that this is not necessarily the case although, during an epidemic, carriage of the epidemic strain does increase.¹⁷

Certainly, the incidence of meningococcal meningitis and meningococcaemia is low among HIV infected individuals, in contrast with infections due to another encapsulated bacteria, *Streptococcus pneumonia*, which occur more frequently in HIV infected individuals than in seronegative controls.¹⁸ The reason for this is unclear. It may be that there is a differential susceptibility to encapsulated bacteria, or that there is a greater activity of complement mediated bacteriolysis with Gram negative organisms. If, however, disseminated meningococcal infection does occur in the presence of HIV infection then, although the presentation may be atypical, the response to antimicrobial therapy is generally good.¹⁸

The culture of yeasts from nasopharyngeal samples occurred frequently and independently from symptoms and was not an indication for treatment. A follow up study of this cohort is in progress. It was interesting that neither toxin nor non-toxin producing *C diphtheriae* were isolated from any of the 327 swabs despite recent trends.^{15 16} No isolates of *N gonorrhoeae* were obtained from the nasopharynx and hence we would question the usefulness of routine screening for oral sexually transmitted pathogens without clinical indications.

Although oro-genital sexual practice seems of material importance in the nasopharyngeal carriage of *N meningitidis* it is possible that the overall nasopharyngeal flora in our recruits may have been influenced by other factors such as the number of different partners each had, the microbiological pattern in their partners, their own smoking history, concurrent medication, or CD4 cell count. Further large study longitudinal data are required.

Although more homosexual men than heterosexual men use condoms for oro-genital sex,¹³ previous reports^{19 20} have suggested that utilisation is generally low and we found no evidence to suggest that the situation has changed. Dental dam use in our study was negligible and others²⁰ have reported that when used it is used once only, as a sex toy or for curiosity, rather than for disease prevention. Like others,²¹ we confirmed that condom use increased when the relationship was known to be discordant, although in our study this did not achieve statistical significance. In addition, information from homosexual men attending "gay" bars and clubs has suggested that self perceptions of how risky one's own sexual behaviour is may be associated with an increase in condom use.¹⁹ The findings from our cohort did not concur with this. Instead, we found that high risk perceptions of HIV transmission by oro-penile sex were associated with abstinence rather than increased condom use.

It appears that there is a small but significant risk of HIV transmission associated with oro-penile sex, particularly for the receptive

partner.^{22,23} As many individuals have adopted oro-genital sex as an acceptable safer sex alternative the relative risks of this should be discussed and, as recommended by the Expert Advisory Group on AIDS, condom use should be advised to increase the safety.²⁴ Nevertheless, with data from Project SIGMA suggesting that at the individual level almost one third of men change their sexual practices over time, with equal proportions increasing or decreasing their risk behaviour, such advice should be given with caution.²⁰ In particular, care must be taken to avoid overstressing the low risks of oro-genital sex and as a consequence it being replaced by higher risk practices.

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